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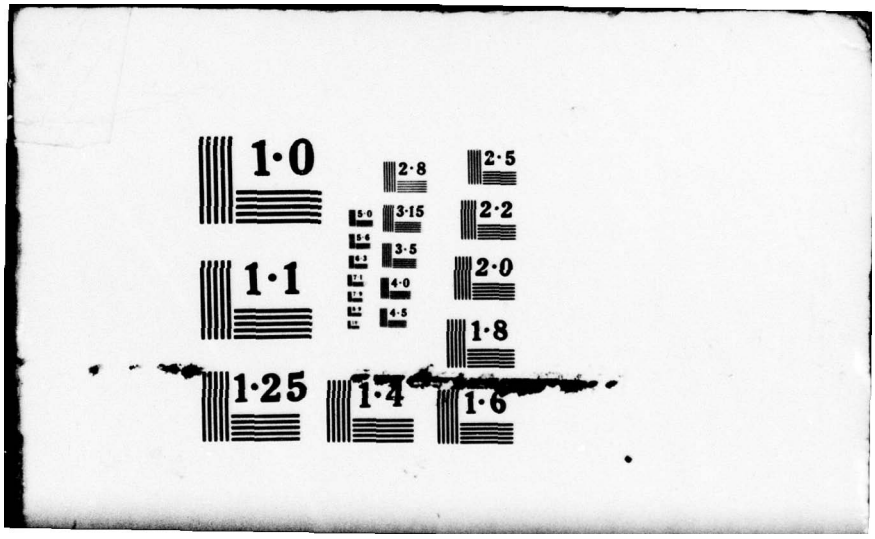
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RELATIONSHIP OF SODIUM IN DRINKING WATER AND TOXEMIA OF PREGNANCY: A PILOT STUDY IN HOUSTON, TEXAS

Master's thesis, by

RICHARD F. JONES, M.D.

June 78

30 p.

PROJECT

Presented to the Faculty of the University of Texas

Health Science Center at Houston

School of Public Health

in Partial Fulfillment

of the Requirements

for the Degree of

MASTER OF PUBLIC HEALTH

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PREFACE

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ACKNOWLEDGEMENT

The author wishes to thank Irina Cech, Ph.D., for her contributions to this effort. Without her suggestions and encouragement this study would not have been performed. Her energy, dedication and availability for consultation will serve as examples to emulate for my entire professional career. The assistance of Drs. Alfonso Holguin and Robert Hardy were also appreciated and their names along with Dr. Cech's will appear on the published study.

ABSTRACT

This study is a retrospective case comparison analysis of the relationship of water-borne Na^+ and toxemia of pregnancy as a part of a continuous investigation at our facility on the role of various water constituents in human chronic disease. Five hundred thirty-seven toxemic women delivered at Jefferson Davis Hospital, Houston, Texas, during 1976 were matched by age, race, parity and month of delivery to 537 non-toxemic controls. Sodium concentration in each patient's drinking water was derived, based on her address, from earlier prepared maps of sodium distribution in Houston's water supplies. Paired t-tests were performed to compare the Na^+ levels which varied from 19 to 250 mg/l in water supplies of cases and controls. Odds ration analysis was used to test for the presence of a gradient in occurrence of toxemia in parallel with the gradient of Na^+. No significant impact of water-borne Na^+ in the indicated range was observed. Further studies incorporating still higher ranges are contemplated.

INTRODUCTION

The passage of the 1974 Safe Drinking Water Act (PL93-523) uncovered rather clearly the need for further information on the role of various water constituents in chronic disease. One of these is the biologically essential sodium ion. There is still considerable divergency of opinion over the need for a sodium standard for drinking water. Although Na^+ in the United States municipal water supplies ranges from less than 20 mg/l to 250 mg/l and higher, there is no clear knowledge of the biological significance of such a range on the population at large. One area of agreement regarding the importance of water-borne Na^+ seems to be for the small segment of the American population who are on severely restrictive diets of less than 500 mg/l total daily intake of sodium prescribed in treatment of severe hypertension, congestive heart failure, cirrhosis, and certain renal conditions. For this population the American Heart Association[1] recommends the limit of 20 mg/l of Na^+ in drinking water. There is in addition a larger segment of the population on milder sodium restriction for less severe medical conditions or who self-impose salt limitations for weight control, presumed health benefits or comfort.

The fact that the relative proportion of Na^+ ingested through food can ordinarily far overshadow the contribution from water makes the study of the health significance of water-borne Na^+ a formidable task. Average daily adult fluid intake ranges from 1.5 to 3 liters,[2] varying with occupation, climate and habit. Total Na^+ intake is reported as 3,000-4,000 mg/day[2] or higher. It is somewhat surprising, therefore, that a recent study by Calabrese and Tuthill[3] was able to detect a significant upward shift in systolic and diastolic blood pressures in a high school population drinking water containing 107 mg/l of Na^+ compared to a similar population exposed to 8 mg/l. The range at which this difference was detected cannot be regarded as unusually large.

In 1976 a survey was made of the Na^+ concentration in Houston, Texas, drinking water by our group. Fifty water supply sources in the city were surveyed and the variation of Na^+ found was considerable, from 19 mg/l in the Northeast section of the city to 250 mg/l in the southeastern part closer to the coast. This problem with salt (NaCl) in community water supplies is apparently not unique. Forty-three states,[4] including 22 inland states,[5] have reported various salt encroachment problems.

The range of Na^+ observed in Houston is more than twice that found to be significant by Calabrese and Tuthill, which prompts a series of questions as to its influence on the health of city residents. At the higher end of this range as

little as eight 8 ounce glasses of water a day would be enough to exceed the 500 mg/day Na^+ limit of severely restricted diets. The number of people on such a diet, however, is relatively small. We chose to concentrate on the larger number of individuals on mild-moderate sodium restriction. One group of diseases for which Na^+ restriction is often prescribed comprises the confusing array of conditions generically referred to as the toxemias of pregnancy, or simply, toxemia, which includes pre-eclampsia and eclampsia.

Toxemia is characterized by the occurrence, during the last half of pregnancy, of varying combinations of hypertension, edema, proteinuria and, occasionally, convulsions and/or coma. Rarely, death of the mother or fetus results. Primiparity and extremes of age are known associations, while study of other variables like socioeconomic status, race, and seasonal changes has yielded conflicting results.[6,7] Historically, an accepted premise has been that sodium intake during pregnancy somehow causes or is related to the severity of toxemia. This resulted in the almost universal restriction of salt in suspected pre-eclampsia and its often prophylactic restriction in normal pregnancies. Recent reports suggest that this practice, beyond being difficult and uncomfortable for the patient, at least may be unnecessary and at worst may be dangerous for the mother and/or fetus.[8] Several clinical studies have shown either no effect

or actual improvement in the toxemic condition when sodium is used as treatment.[9-14] Despite these reports, salt restriction remains a widespread practice in the treatment of preeclampsia and many non-toxemic pregnant women are forced to endure long periods of unpleasant low salt diets in an attempt to prevent development of preeclampsia.

It was our opinion that further information as to the role of Na^+ in the development and course of toxemia was necessary. The existence of a comparatively large range of Na^+ in the drinking water of the Houston area was felt to offer a natural laboratory setting for the study of the relationship of water-borne Na^+ to this condition.

EXPERIMENTAL DESIGN

Population and Setting

The study population was pregnant women delivered at Jefferson Davis Hospital (J.D.H.), Houston, Texas, during 1976. This is the only obstetrical hospital for Harris County, Texas. During 1976, over 10,000 live births were registered in this facility and more than 1,100 cases of toxemia were recorded. This particular hospital is the only one in Houston with a large enough volume of deliveries and cases of toxemia to allow a statistically valid sample to be obtained from a single institution. This reduces the difficulties of

inconsistently applied criteria and noncomparability of patient populations and data encountered by other investigators using information from more than one hospital. The hospital is associated with 12 neighborhood outpatient clinics providing prenatal care located in all major areas of the city and patients are widely distributed geographically. The county health delivery system serves a greater proportion of Blacks and Mexican-Americans than is present in the general population of the local area. Fifty-six percent of the patients are judged capable of paying the entire cost of obstetrical care, but essentially all of the patients are at the lower end of the socioeconomic scale.

Sampling

This study was a retrospective case comparison analysis of data obtained by review of hospital and outpatient clinic records. All available 1976 records designated by the International Classification of Disease Code, eighth revision as 637.0 (pre-eclampsia), 637.1 (eclampsia) and 637.9 (toxemia, unspecified) were reviewed. Controls were randomly selected and carefully matched to cases for age, parity, race and month of delivery from those records labeled 650.0 (uncomplicated pregnancy). See Figure 1 for a breakdown of matching categories.

In addition to patient descriptive information, all charts were examined for appropriate blood pressure data, physician diagnosis, extent of proteinura and/or edema, prenatal salt restriction or bed rest and prenatal use of sedatives or diuretics. Potential toxemic cases were also reviewed for a second elevated blood pressure at least six hours after the first and specific treatment for toxemia.

Inclusion Criteria

The most commonly used criteria for the diagnosis and classification of toxemias of pregnancy in the United States are the recommendations of the American Committee on Maternal Welfare as presented by Hellman and Pritchard.[17] By these criteria preeclampsia is defined as the presence singly or in combination, after the twentieth week of gestation, of an increase in blood pressure on at least two occasions six hours apart or more, generalized edema (edema of more than legs) and proteinuria. Elevated blood pressure is defined as a rise of 30 mm Hg systolic or an absolute systolic of 140 or a rise of 15 mm Hg diastolic or an absolute level of 90 or above. Eclampsia assumes the occurrence of convulsions or coma superimposed on the symptoms of preeclampsia.

For a case of preeclampsia to be included in this study the blood pressure at diagnosis had to meet or exceed the limits recommended by the National Committee on Maternal Welfare.

If labor lasted longer than six hours, the blood pressure at that point had to also be elevated, but patients were included if all recorded blood pressures during labor were elevated even though the period of observed labor lasted less than six hours. The patient's blood pressure had to have returned to normal by the time of discharge from the hospital to reduce the possibility of including chronic hypertensives in the study population. A diagnosis of preeclampsia, toxemia or eclampsia had to be made by a physician but, in addition, evidence was necessary that the physician had acted upon his diagnosis and changed his course of treatment to specifically address toxemia. Any mention in the record of pre-existant hypertension, renal disease other than mild pyelonephritis, or diabetes mellitus other than Class A, caused the case to be discarded.

Controls were included if review of the records proved the patient to be free of the same complicating diseases as cases. Blood pressure had to be normal during confinement, although transient elevations during labor were allowed. The presence of edema or proteinuria did not exclude the patient.

At no time during the data gathering process did the data collector know the actual distribution of Na^+ in the water supplies of the city. Any chart where the patient's address changed during the prenatal period was eliminated. Only the data collector had access to the patient's address. Assignment of

a Na^+ level to each address was accomplished in a double blind fashion by two investigators, one calling out the address without indicating whether it was case or control, the other providing the Na^+ level to match the address.

RESULTS

The total number of records reviewed for potential toxemia was 1,036 from which 150 patients were culled for co-morbid conditions (primarily chronic hypertension - 133 cases) and 163 patients were eliminated for not otherwise meeting the study criteria for inclusion (i.e. no elevated blood pressures or only transient rise in blood pressure recorded). An additional 57 patients resided outside of the study area and 44 records were either incomplete or the patient did not actually deliver in 1976. A total of 2,022 records were examined as potential controls. Of these, 1,051 did not meet one or another of the matching criteria; 245 appeared to actually be cases of toxemia (most were miscoded by the records section); 12 had exclusionary co-morbid conditions, 95 were from out of the study area and 82 records were incomplete or deliveries did not occur in 1976.

Overall, we were able to match 537 of the available 622 cases to similar controls. The matched pairs consisted of 300 Blacks, 122 Mexican-Americans and 115 Whites. There were

394 G_1P_o's, 18 G_2P_o's, 120 G_{2-4}'s and five patients with parity of five or greater. The age distribution of case-control pairs by category was: 11-15(60), 16-20(359), 21-25(87), 26-30(26), and 30-35(5) with the mean age of cases being 18.99 and that of controls being 18.84. Figure 1 illustrates matched characteristics of the study population. Among the cases there were six occurrences of eclampsia and 44 cases were labeled as severely toxemic; the remainder were referred to as preeclampsic or toxemic. Four fetal deaths were recorded among the cases and one among the controls. There were no maternal deaths. There were five twin deliveries for cases and one for controls. There were 117 cesarian sections performed on cases for a ratio of 21.79% with ten being done for singleton or twin breech and the remainder for other indications, five of which seemed to be for toxemia alone. For the controls only three cesarian sections were performed, one for breech, one repeat and one for failure to progress. Eighty-one percent of cases and 79% of controls received some prenatal care.

Means were calculated for all blood pressures obtained (Figure 2). Mean prenatal systolic blood pressure for cases was 115.91 and for controls was 110.21 while mean prenatal diastolic blood pressure was found to be 69.25 for cases and 65.97 for controls. Mean systolic blood pressure at discharge was

116.64 for cases and 111.28 for controls with diastolic mean values of 75.89 and 71.42 respectively. Case means for systolic blood pressure at diagnosis and at six hours later or greater were 142.35 and 143.42 respectively with corresponding mean diastolic values of 93.81 and 95.29. The mean of the highest recorded systolic blood pressure for controls was 129.55 while the mean highest diastolic blood pressure mean was 83.28. Paired t-tests were performed to examine comparable blood pressures for cases and controls. All comparisons showed case values to be significantly higher than controls at the .001 level of probability or better (Table 1).

Mean sodium value in drinking water for cases was 79.49 and for controls was 81.18 mg/l. Paired t-tests showed these mean levels not to differ significantly (t-value = -0.77, P = 0.441). Sodium values were then divided into five categories: 0-39, 40-79, 80-119, 120-159 and 160+ mg/l. Odds ratio analysis was performed for these categories which did not show a gradient in occurrence to toxemia (Table 2). Pairing was disregarded in this and subsequent odds ratio analyses because the pairing produced only a negligible correlation in the responses for cases and controls (phi coefficient 0.029). Odds ratio analysis was then done comparing the 0-39 mg/l category (lowest Na^+) to the combined categories 40 mg/l + (higher Na^+) because of the lack of a gradient (Table 3). This odds ratio was 1.23 with confidence limits of 0.93 to 1.62

($x^2 = 2.04$, $P > 0.10$). Similarly no gradients were found when analysis by odds ratio for all sodium categories was done controlling for age, parity, or race, thus odds ratios were calculated for these subgroups comparing the 0-39 mg/l group to the combined remaining categories. No significant relationships were found.

DISSCUSSION

In order to most effectively study the influence of a water-borne constituent on any disease, it is necessary to select a patient population whose drinking water source is consistent. The obstetrical patients served by J.D.H. comprise such a population. Essentially none of these patients work and their level of income precludes much of their budget being allocated to dining out or buying bottled water. The state of pregnancy decreases the patient's mobility further reducing the likelihood of water coming from sources other than the home and its immediate surroundings. In addition, all outpatient clinic patients were given prenatal diet instructions which included recommendations to increase protein intake while decreasing carbohydrate and salt intake. It was, therefore, felt that while there would be a variation in Na^+ intake through food, this dietary counseling would tend to reduce the range and mean

of food-borne Na^+ thus making the relative proportion of Na^+ contributed by water of more importance than it is in the general population.

The selection of inclusion criteria for this study was a difficult task. Preliminary study of sample records showed that more than half lacked urine protein results and/or mention of edema on admission physical exam. Some investigators have shown proteinuria and edema to be unreliable and not of particular value in the diagnosis of toxemia,[18,19,20] so it was felt reasonable not to base inclusion on these findings.

Diagnosis was further complicated by the fact that frequently the first elevated blood pressure of a pregnant patient is observed when she presents for delivery and by the time six hours have passed she has been long delivered and the blood pressure has returned to normal. All of the above factors made it difficult in many cases to meet the established criteria and required the application of additional guidelines for inclusion. Our criteria therefore centered primarily around blood pressure and had to rely heavily on physician diagnosis and resultant treatment to delineate cases and controls. Thus, it is not surprising that the two populations exhibit highly significant differences in mean confinement blood pressures. It is interesting, however, that the two populations can also be separated statistically by blood pressure during the prenatal and postnatal

periods with the toxemic population having significantly higher mean values than controls in both instances, although none of these means were outside normal limits.

Due to the retrospective nature of the study, no strong inferences can be made as to the average dietary salt intake for each group or for subgroups. Intuitively, one would expect ethnic and age differences in habitual intake of salt. In a recent study of a predominantly Black low income pregnant population a mean daily unrestricted Na^+ intake of less than 2,000 mg was determined by 24 hour diet recall.[21] Another study found an average daily Na^+ intake of 4,200 mg when free use of salt was allowed in a group of white, unmarried, pregnant women.[22] No comparable data for Mexican-American women could be located. We feel fairly safe in assuming an average intake of sodium from food in our study population to be about 4,000 mg/day or less. Therefore, using 3 l as the average amount of water consumed daily in a hot climate like Houston's through drinking and cooking, the contribution of water-borne Na^+ would range from 1.5 to 16 percent respectively for the lowest and highest values of sodium in the domestic water of Houston. The average woman in our study would have received six percent of her daily Na^+ from water. Even though those percentages are not very large, if one hypothesizes a direct relationship between Na^+ and either aggrevation of or protection against

toxemia one would expect to see a gradient, although perhaps small, in the odds ratios comparing cases and controls. This was not seen to be the case. Regardless of how one explains this lack of gradient, i.e. no influence of Na^+ on toxemia, not a large enough range of Na^+ in the water of the study area, or Na^+ in food overshadowing the effect of water-borne Na^+, the very narrow confidence limits that resulted when the 0-39 mg/l range was compared to the remaining ranges bespeaks an adequate overall sample size. Certain subgroups, i.e. $Na^+ > 160$ mg/l, age 30-35, $G > 4$, however, were too small for meaningful analysis.

CONCLUSION

In view of the odds ratio analysis and paired t-test results we feel confident in stating that water-borne Na^+, in the range studied, had no influence on the occurrence of toxemia of pregnancy in this population examined as a whole. An attractive opportunity exists near the present study area to test the effects of still larger ranges. The coastal cities southeast of Houston including Baytown, Galena Park, Deer Park and Pasadena have sodium levels in their well water nearing 450 mg/l and are also served by Jefferson Davis Hospital. It is our intention to gather another two year's data incorporating these communities.

The resulting expanded sample size will allow more intensive subgroup analysis thereby increasing the likelihood of uncovering any influence of water-borne Na^+ in this disease, should one exist.

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TABLE 1.

COMPARISON OF SIMILAR CATEGORIES OF
BLOOD PRESSURES FOR CASES AND CONTROLS
BY PAIRED t-TEST

Blood Pressures Compared		N	t Value	Two Tail Probability
Earliest Prenatal (Cases and Controls)	Systolic	349	5.67	< .001
	Diastolic	349	3.49	.001
At Diagnosis (Cases) Highest (Controls)	Systolic	537	18.52	< .001
	Diastolic	537	20.15	< .001
>6 Hr After Diagnosis (Cases) Highest (Controls)	Systolic	411	18.11	< .001
	Diastolic	411	20.82	< .001
Last (Cases and Controls)	Systolic	536	10.68	< .001
	Diastolic	536	8.26	< .001

TABLE 2

ODDS RATIO ANALYSIS OF NA^+ LEVELS FOR CASES AND CONTROLS BY NA^+ CATEGORIES

Na^+ Category (mg/l)	N (Cases)	N (Controls)	Odds Ratio
0-39	139	119	1.0
40-79	75	92	1.43
80-119	244	252	1.21
120-159	74	68	1.07
160 +	5	6	1.40

TABLE 3.

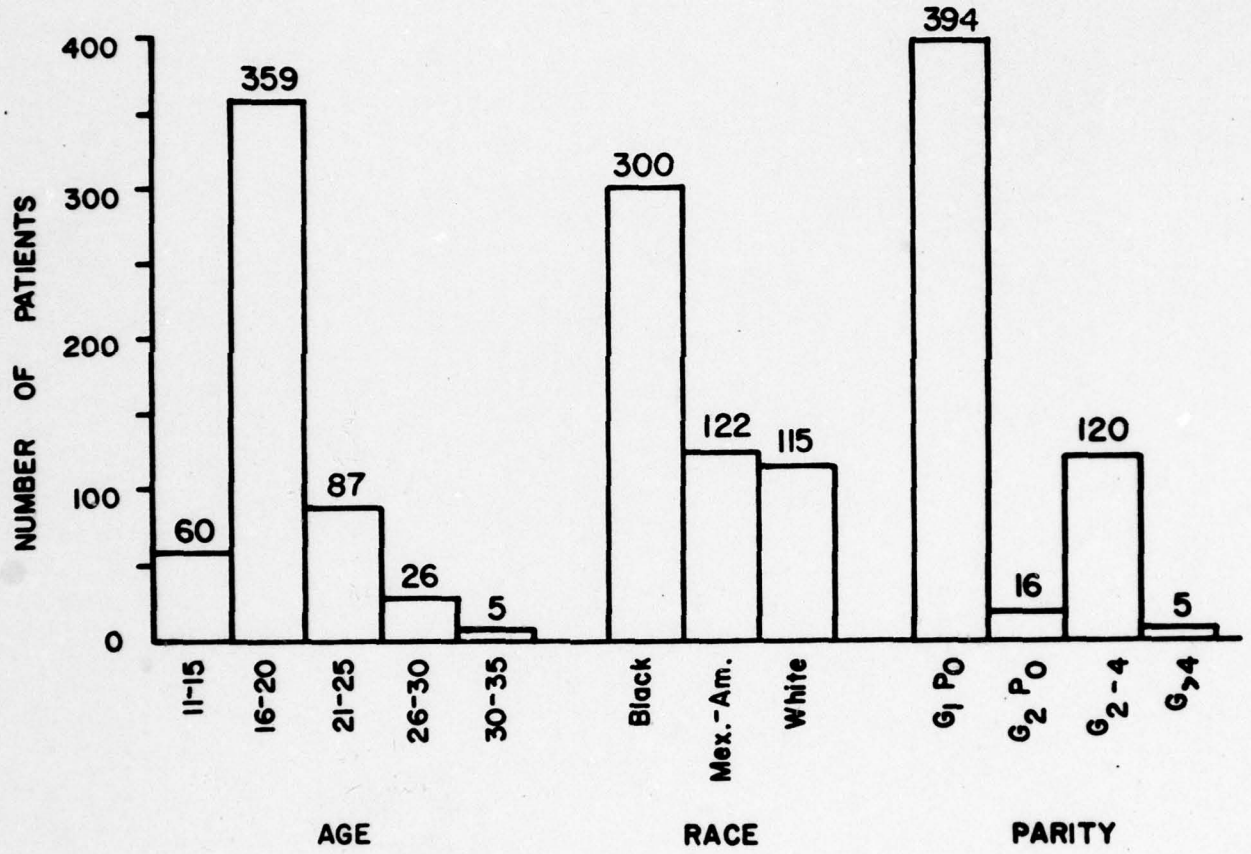
ODDS RATIO ANALYSIS FOR LOWEST NA^+ CATEGORY COMPARED TO COMBINED HIGHER CATEGORIES

Na^+ Category (mg/l)	N (Cases)	N (Controls)	Odds Ratio	X^2	P
0-39	139	119			
40+	398	418	1.23	2.04	>0.10

FIGURE CAPTIONS

Figure 1. Matched characteristics and numbers of cases and controls by age, race and parity (G_x = x pregnancies, P_x = x live births).

Figure 2. Means and ranges of blood pressure for cases and controls.


NUMBER OF PATIENTS
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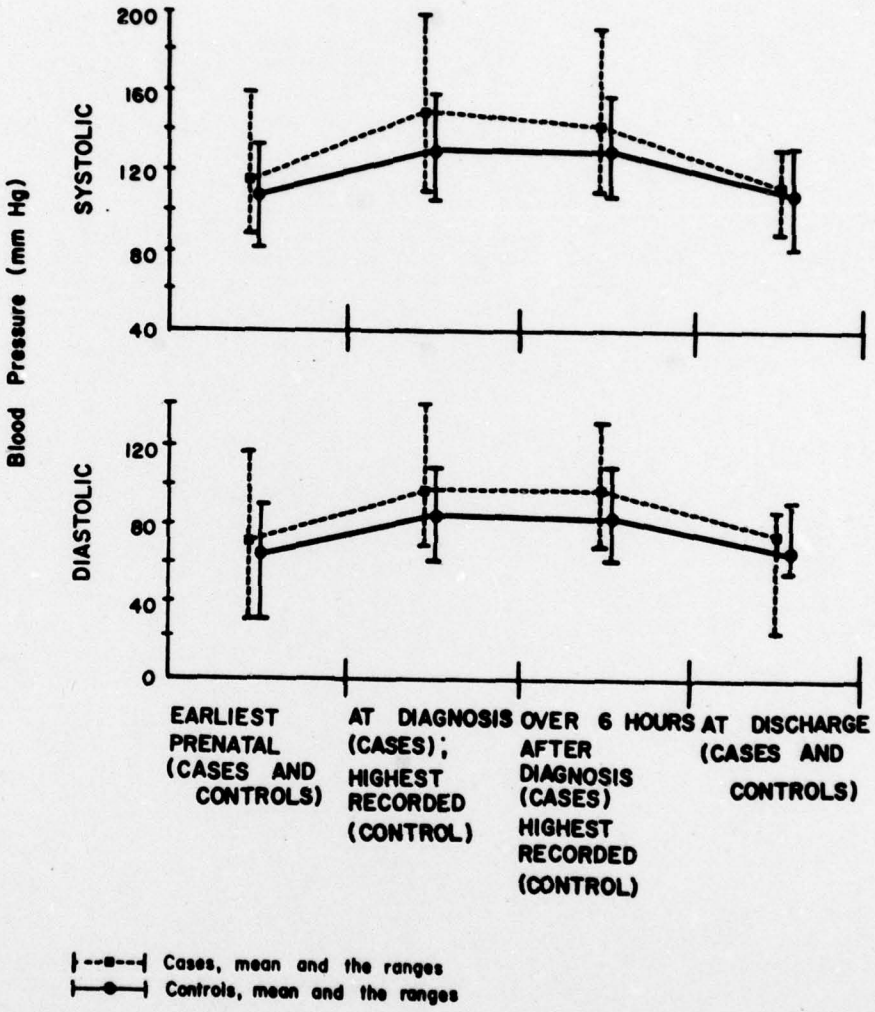
300
200
100
0
60
359
87
26
5
300
122
115
394
16
120
5
11-15
16-20
21-25
26-30
30-35
Black
Mex.-Am.
White
G1 P0
G2 P0
G2-4
G>4
AGE
RACE
PARITY


Blood Pressure (mm Hg)
SYSTOLIC
200
160
120
80
40
DIASTOLIC
120
80
40
0
EARLIEST PRENATAL (CASES AND CONTROLS)
AT DIAGNOSIS (CASES); HIGHEST RECORDED (CONTROL)
OVER 6 HOURS AFTER DIAGNOSIS (CASES) HIGHEST RECORDED (CONTROL)
AT DISCHARGE (CASES AND CONTROLS)
Cases, mean and the ranges
Controls, mean and the ranges

VITA

Richard Francis Jones was born in Iron Mountain, Michigan, on November 13, 1944, the son of Richard Francis Jones and Janice Elaine Frangquist. After completing his work at Lincoln High School, Manitowoc, Wisconsin, in 1962, he entered the University of Wisconsin at Madison. After a break in college from June, 1965, to December, 1968, to serve as an aeromedical technician in the Air Force he returned to the University of Wisconsin to major in zoology, receiving the degree of Bachelor of Science in January, 1970. During the following year he was employed by State Farm Insurance Company as a bodily injury claims adjuster. The next one and one-half years were spent at Arizona State University, Tempe, Arizona, in graduate education in zoology, but this course of study was interrupted by acceptance at the University of Arizona College of Medicine at Tuscon culminating in the attainment of a Medical Degree in June, 1975. He entered the Air Force Health Professions Scholarship Program in 1973 and entered active duty at Wright-Patterson Air Force Base, Ohio, for one year of internship ending in June, 1976.

After a short period of additional training at The School of Aerospace Medicine, Brooks Air Force Base, Texas, he was assigned as a flight surgeon to the SR-71 and U-2 squadrons

at Beale Air Force Base, California. He entered the School of Public Health at the University of Texas in September, 1977, to complete the first year of his Aerospace Medicine Residency. As of July, 1978, he will be assigned once again to the School of Aerospace Medicine in San Antonio, Texas, to complete the final year of his residency.

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This thesis was typed by Nancy Lee Harris.